Hepatitis B

CDNA National Guidelines for Public Health Units

Revision history			
Version	**Date**	**Revised by**	**Changes**
1.0	21 March 2017	Katrina Knope Mark Veitch	Incorporated CDNA comments

The Series of National Guidelines ('the Guidelines') have been developed by the Communicable Diseases Network Australia (CDNA) and endorsed by the Australian Health Protection Principal Committee (AHPPC). Their purpose is to provide nationally consistent guidance to public health units (PHUs) in responding to a notifiable disease event.

These guidelines capture the knowledge of experienced professionals and provide guidance on best practice based upon the best available evidence at the time of completion.

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1. Summary

Public health priority

High for newly acquired cases; routine for those with chronic infection and unspecified cases.

Note: The terms *acute* and *chronic* refer to the two typical clinical presentations of hepatitis B virus (HBV) infection. The National Notifiable Disease Surveillance System (NNDSS) case definitions refer to *newly acquired* cases, which is largely synonymous with acute infections; and *unspecified cases*. *Unspecified* cases are likely to be mostly chronic infections but a small proportion may be acute.

Case management

Individual clinical case management is the responsibility of the treating clinician. Public health units (PHUs) should determine if the case is newly acquired and where possible, identify potential source/s of exposure.

Contact management

The jurisdictional or regional PHU will engage with the treating clinician, to identify contacts of both newly acquired and unspecified infections; and to support the treating clinician to minimise the public health consequences of HBV infection through counselling, additional testing, post-exposure prophylaxis and/or vaccination of non-immune contacts.

2. The disease

Infectious agents

HBV is comprised of a number of clinically and diagnostically important viral proteins. These include the envelope protein hepatitis B surface antigen (HBsAg), hepatitis B core antigen (HBcAg), and a soluble nucleocapsid protein, hepatitis B e antigen (HBeAg).
Eight genotypes of HBV have been identified (A to H) that have different geographical distributions and clinical outcomes. The more common genotypes in Asia are B and C; and in Europe, the Middle East, and India, A and D. The distribution of genotypes in Australia is less well defined, but the range of genotypes present is likely to reflect the migration patterns from high prevalence countries. Genotype C4 is prevalent among Aboriginal communities in Northern Australia (1,2).

Reservoir

Humans are the only known natural host. People with chronic infections are the major reservoir of infection.

Mode of transmission

HBV is transmitted via parenteral, percutaneous (broken or penetrated skin) or mucosal exposure to infectious body fluids (blood, vaginal fluids, semen and saliva if contaminated with blood) of an infected person. An extremely small volume of blood may be sufficient to transmit infection because of the high concentration of virus in blood in some individuals. Viral concentrations in blood can exceed 10 billion HBV DNA international units per ml (IU/mL) (3). The minimum infectious dose in experimental conditions has been estimated to be approximately 10 HBV DNA copies (4).

Historically, the risk of HBV transmission from a patient to an uninfected person has been linked to the hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg) status of the source patient.

In studies of health care workers (HCWs) who sustained needle stick injuries (NSIs) from sharps contaminated with blood containing HBV, the risk of seroconversion for HBV infection ranged from 37 per cent to 62 per cent if the source patient was both HBsAg-positive and HBeAg positive, and 23 per cent to 37 per cent if the source was HBsAg-positive but HBeAg-negative [9,12]. The risk of developing clinical hepatitis after exposure ranged from 22 per cent to 31 per cent if the source patient was both HBsAg-positive and HBeAg positive, and from 1 per cent to 6 per cent if the source was HBsAg-positive but HBeAg-negative (5, 6).

As viral load monitoring becomes more common, these risks will be re-evaluated using new data. In general, higher viral loads in a source patient have been associated with increased probability of seroconversion in a recipient (7).

Modes of transmission include:

- Perinatal transmission from an infected mother to her infant.
- Percutaneous or parenteral exposure to infected blood and other bodily fluids in scenarios including:
    - sharing and reusing contaminated objects that pierce the skin or mucous membranes, such as needles, syringes, injecting fluids and other equipment associated with injecting drug use (IDU), tattoo equipment, body-piercing equipment, acupuncture equipment, razor blades, toothbrushes and manicure/pedicure instruments such as nail clippers
    - needle-stick injuries
    - transfusion of infected blood or blood products. The Australian Red Cross Blood Service commenced screening for HBsAg in July 1971 and have used HBV DNA screening since 2010
    - invasive medical or dental procedures if there has been inadequate infection control
    - human bites
    - direct contact through non-intact skin with the blood or open sores of an infected person.
- Mucosal exposure to infected blood and other bodily fluids in scenarios including:
    - sexual contact
    - contact between infectious body fluid and mucous membranes, such as a splash of blood into eyes or mouth.

Transmission occasionally occurs in settings, such as households, through non-sexual contact with an infected person, but where the precise mode of transmission is unclear. Overcrowded homes increase this risk where there are more people and hence more chances of contact and exposure with an infected person.

The risk of transmission of hepatitis B may also be increased in settings where there is a high prevalence of violence and injury, or where cultural practices involve exposure to blood.

There is no evidence for HBV transmission by:

- breast feeding (8)
- faecal-oral transmission
- insect vectors
- kissing coughing or sneezing
- sharing food or eating utensils
- skin to skin contact, provided skin is intact
- saliva, unless visibly contaminated by blood or inoculated directly into tissues (9-13).

Incubation period

The incubation period varies from 45 to 180 days (14) and most commonly is 60 to 90 days. The incubation period depends on the amount of virus in the inoculum, mode of transmission, and host factors.

Infectious period

Infectivity during acute infections in adults commences several weeks before the onset of symptoms and usually lasts four to five months while HBsAg is present in blood and other secretions (3). People with chronic infection usually remain infectious for life (15).

Clinical presentation and outcome

Only 30 to 50 per cent of adults and less than 10 per cent of children with acute HBV infection have symptoms. In neonates and young children, particularly those less than one year of age, initial infection is usually asymptomatic. When symptoms are present, they can have an insidious onset and include:

- anorexia
- fever
- jaundice
- dark-coloured urine
- light-coloured stools
- vague abdominal discomfort
- malaise
- nausea and vomiting.

In 1-10 per cent of acute HBV infections, jaundice may be preceded by an acute fever, arthralgia or arthritis and skin rash. Fulminant hepatitis causing acute liver failure occurs in <1 per cent of acute HBV infections (16). Survival rates for acute liver failure depend on the nature and reversibility of the cause of liver failure, the likelihood of spontaneous hepatic recovery, and access to specialist care in tertiary health services. Studies of patients managed in specialist liver clinics in the USA show more than half of all-cause acute liver failure cases survive (17, 18).

During recovery from HBV infection malaise and fatigue may persist for many weeks.

Following acute infection, approximately five per cent of people infected in adulthood, but up to 95 per cent of neonates and 20-30 per cent of children aged one to five years, become chronically infected with HBV (19, 20).

Chronic HBV infection is defined as detection of HBsAg more than six months after prior evidence of infection. Chronic HBV infection is generally asymptomatic until clinical signs of complicated liver diseases such as cirrhosis, portal hypertension or hepatocellular carcinoma become evident. Four successive phases of variable duration have been described for chronic infection: immune tolerance, immune clearance, immune control and immune escape (21). The Gastroenterological Society of Australia website (note that the urls for hyperlinked resources are provided in the section *Further information*) provides a recent clinical update on chronic hepatitis B (CHB). Progression of liver disease due to chronic HBV infection may be:

- promoted by co-infection with human immunodeficiency virus (HIV), or other forms of immunocompromise
- promoted by co-existing chronic liver disease due to alcohol and/or hepatitis C or D (22).
- delayed (and reversed) by treatment (23-25).

Premature mortality due to cirrhosis and/or hepatocellular carcinoma is associated with up to 25 per cent of cases of long-term chronic infection (26). Most people diagnosed with liver cancer in Australia die within one to two years (27).

People at increased risk of infection

In Australia, the following populations are most at risk of acute hepatitis B:

- Infants born to mothers with CHB, especially if not immunised at birth
- Household contacts of people infected with HBV
- Sexual contacts of people infected with HBV, including men who have sex with men (MSM) (28)
- People who share needles, syringes, injecting fluids and other injecting equipment
- Sexual contacts of a person who is an injecting drug user
- People who work in high-risk occupational settings such as healthcare, correctional facilities, laboratories, mortuaries, ambulance or police work, or employment in facilities for the intellectually impaired.

Uncommonly in Australia, acute HBV infection can be identified as linked to the following settings:

- Haemodialysis
- Tattooing, body-piercing or acupuncture without adequate infection control
- Needle stick injury
- Accidental exposure of the eyes, mucous membranes or a wound to the blood of another person
- Blood transfusion - now rare, but risk may occur due to the pre-seroconversion window period, infection with immunovariant viruses or occult HBV
- Receiving blood transfusions or other blood products, dental or surgical care in overseas settings with poor infection control, especially in areas with high hepatitis B prevalence.

In Australia, the following populations (with historical and/or current high prevalence of infection) are most at risk of CHB:

- People born in an intermediate or high hepatitis B prevalence country (largely through perinatal or early childhood infection)
- Aboriginal and Torres Strait Islander people (particularly adults infected perinatally or in early childhood before universal vaccination)
- Infants born to mothers with CHB, especially if not immunised at birth
- People with developmental disabilities (29, 30)
- People living with human immunodeficiency virus (HIV) or hepatitis C virus (HCV)
- People who have ever been incarcerated in a custodial setting.

Disease occurrence and public health significance

Between 2010 and 2015, the notification rate of newly acquired hepatitis B in Australia ranged from 0.6 to 1.1 per 100,000 population. Since 2006, the rate of diagnosis of newly acquired infections has declined across all age groups, with the greatest declines observed among people aged 15-24 years (31). This age-specific decline in hepatitis B notifications is attributable to the HBV vaccination programs introduced nationally from 1997 in adolescents, and infants from 2000.

Notified newly acquired cases of HBV infection in Australia occur mostly in adults aged 25 to 39 years of age, and are most often attributed to injecting drug use, sexual contact and occasionally skin penetrating procedures (31).

The reliability of notification data for informing estimates of incidence and prevalence, newly acquired and chronic infections is limited due to the nature of the disease. Most new HBV infections are asymptomatic and go undetected. Detection of chronic infections relies on regular screening in at risk populations.

Higher rates of hospitalisation, mortality and morbidity from HBV infection have been reported among Aboriginal and Torres Strait Islander people compared with the general Australian population. In 2015 the notification rate of newly acquired HBV infection in the Aboriginal and Torres Strait Islander population was more than three times that in the non-Indigenous population (31).

The overall prevalence of CHB in the Australian population is relatively low for our region, but the number of people living with CHB continues to increase. Between 2006 and 2015 the annual rate of unspecified hepatitis B notifications remained relatively stable ranging between 26.8 and 32.1 per 100,000. It is estimated that 239,200 people (approximately 1 per cent of the population) were living with chronic HBV in 2015, of whom approximately 38 per cent remained undiagnosed and only 6.1 per cent were receiving antiviral treatment (32).

Most primary liver cancer is attributable to chronic viral hepatitis. The annual number of new cases of liver cancer recorded in Australian cancer registries almost tripled between 1982 and 2007 (from 1.8 to 5.2 cases per 100 000 population), and while the notification rate of unspecified hepatitis B is currently stable, the burden of CHB is expected to increase.

Given current access to treatment and care (with low rates of antiviral administration) the number of cases of hepatitis B related liver cancer is expected to continue to grow (27). Of people living with chronic hepatitis B in Australia, an estimated 56 per cent are people born overseas, 9 per cent are Aboriginal and Torres Strait Islander people, 5 per cent people who inject drugs (PWID) and 4 per cent men who have sex with men (MSM) (33).

Higher prevalence of chronic HBV infection occurs in Mediterranean countries, parts of eastern Europe, Africa, Central and South America (one to five per cent of population chronically infected), and in many sub-Saharan African, East and Southeast Asian and Pacific island populations (around 10 per cent population chronically infected).

In regions of intermediate (two to seven per cent of the population is HBsAg-positive) to high prevalence of HBsAg ($\geq$8 per cent of the population is HBsAg-positive) infections are mainly acquired perinatally or in early childhood.

Australia is within the WHO Western Pacific Region (WPRO), which has the highest burden of HBV related cirrhosis and liver cancer in the world; many countries have >8% prevalence of HBsAg in their adult population, although in a number of countries (including China) very high levels of infant hepatitis B vaccination have been achieved, resulting in a profound reduction in hepatitis B prevalence among those born in recent decades. Reliable epidemiological estimates for hepatitis B are not available for many countries in the region, however WPRO maintains hepatitis data and statistics summarising prevalence of HBsAg and HCV RNA in selected countries.

3. Routine prevention activities

Vaccination

Serum derived HBV vaccines and the recombinant HBV vaccines became available during the 1980s. Some vaccination of infants and high-risk people commenced in Australia in the 1980s. Universal infant vaccination commenced in the Northern Territory in 1990. The adolescent program commenced in states and territories in the mid to late 1990s and the universal infant program, which includes a dose given at birth, began nationally in May 2000. For details of the introduction of hepatitis B vaccination in Australia, refer to the National Centre for Immunisation Research and Surveillance (NCIRS) website.

The Australian infant schedule consists of a dose of monovalent hepatitis B vaccine given at birth, followed by hepatitis B-containing combination vaccine given at 2, 4 and 6 months of age. For information on hepatitis B vaccination refer to *The Australian Immunisation Handbook*.

Risk mitigation

The risk of transmission of HBV is reduced by:

- Screening donated blood and tissues
- Routine antenatal screening of pregnant women for HBsAg, which enables:
    - management to prevent newborn infants developing HBV infection (Table 2, below);
    - follow-up and management of mothers who have chronic HBV infection; and
    - identification of the HBV status of other family and household members, protection of those who are susceptible to HBV infection.
- Universal infant hepatitis B vaccination, including the birth dose
- Vaccination of people at increased risk of infection because of lifestyle, country of birth, Aboriginal and Torres Strait Islander status, medical history, occupation, or sexual, household or household-like or other ongoing intimate contacts with a HBV infected person. This includes household members of the adoptive family if the adopted child is known to have CHB infection
- Infection control in all healthcare settings and in regulated premises where skin penetrating activities occur, refer to the NHMRC Australian Guidelines for the Prevention and Control of Infection in Healthcare (2010).
- Promotion of safer sex practises
- Promotion of safer injecting drug use practises, provision of sterile injecting equipment (via needle and syringe programmes) and opioid substitution treatment programmes
- Education of the case or care-giver about the nature of the infection and the mode of transmission (refer to Education in 9. Case management, below)
- Cleaning up blood spills, refer to Staying Healthy*: Preventing infectious diseases in early childhood education and care services*, 5th Edition
- Avoiding contact with blood or other body fluids and not sharing items potentially contaminated with blood (such as toothbrushes and razors)
- Access to guideline-based primary healthcare, and specialist care where required, including provision of treatment. Appropriate management improves individual health outcomes, engages the individual with the healthcare system and facilitates testing and vaccination of contacts, allows consideration of expanded approaches to prevention of mother to child transmission in pregnant women, and reduces infectivity among those receiving antiviral therapy.

4. Surveillance objectives

Surveillance of hepatitis B aims to collect data to monitor epidemiological trends in hepatitis B, with particular regard to time, place, population groups, and risk factors. These data are used to identify and characterise clusters of cases; inform and evaluate policies, interventions and services to reduce the transmission and consequences of HBV infections; and contribute to reporting on the progress of national strategies.

5. Data management

Confirmed cases should be entered into notifiable diseases database within five working days of notification.

Core data and (for newly acquired cases) enhanced data sought from clinicians and laboratories should be entered as soon as information becomes available. Core and enhanced data from jurisdictions are collated in the NNDSS and by the Kirby Institute. These data are defined in the national core and enhanced hepatitis B datasets. Appendix 2 has a sample case report form based on these specifications for use by PHUs. This data form allows the collection and entry of data additional to that captured by the NNDSS core and enhanced datasets, providing an opportunity to further classify cases and gather additional data on unspecified cases. The extent to which jurisdictions collect data beyond the minimum core and enhanced datasets will depend on resource availability.

6. Communications

Laboratories and/or clinicians diagnosing cases of hepatitis B are required to notify the relevant state and territory health authorities in accordance with the relevant legislation or regulations.

7. Case definition

Only confirmed cases of HBV infection are notifiable.

Hepatitis B – newly acquired

Reporting

Only confirmed cases should be notified.

Confirmed case

A confirmed case requires laboratory definitive evidence only.

Laboratory definitive evidence

Detection of hepatitis B surface antigen (HBsAg) in a patient shown to be negative within the last 24 months

OR

Detection of HBsAg and IgM to hepatitis B core antigen, except where there is prior evidence of hepatitis B infection

OR

Detection of hepatitis B virus by nucleic acid testing, and IgM to hepatitis B core antigen, except where there is prior evidence of hepatitis B infection.

Note: Transient HBsAg positivity can occur in patients following HBV vaccination. This occurs more commonly in dialysis patients and is unlikely to persist beyond 14 days post-vaccination.

Hepatitis B – unspecified

Reporting

Only confirmed cases should be notified.

Confirmed case

A confirmed case requires laboratory definitive evidence AND that the case does not meet any of the criteria for a newly acquired case.

Laboratory definitive evidence

Detection of hepatitis B surface antigen (HBsAg), or hepatitis B virus by nucleic acid testing, except where there is prior evidence of hepatitis B virus infection.

Note: Transient HBsAg positivity can occur in patients following HBV vaccination. This occurs more commonly in dialysis patients and is unlikely to persist beyond 14 days post-vaccination.

Case definitions can be found on the Department of Health's case definitions website.

The Public Health Laboratory Network of Australia (PHLN) has developed laboratory case definitions for recent, chronic and unspecified hepatitis B infection. Refer to the Department of Health PHLN web page.

8. Laboratory testing

Testing Guidelines

The National Hepatitis B Testing Policy provides information about indications for HBV testing, informed consent and conveying test results, refer to the ASHM website. It addresses testing in particular settings (Healthcare Workers, Antenatal and Perinatal Testing, People from Culturally and Linguistically Diverse Backgrounds, and Aboriginal and Torres Strait Islander Peoples) where barriers (such as poor access to primary healthcare, stigma/discrimination, non-English language and inadequate health literacy) have the potential to impede testing of higher risk populations.

Participation in testing is voluntary except in circumstances when testing is mandatory for participation in certain activities or to have access to certain services (such as blood, tissue and organ donation, migration health requirements, entering training or service in the armed forces).

Who to test

Recommend testing based on an individual's risk of HBV infection, refer to *People at increased risk of infection* (Section 2, above) and the National Hepatitis B Testing Policy.

Note also the recommendation for universal screening of pregnant women, refer to the RANZCOG statement.

Testing is also recommended in other situations, such as:

- Health care workers who perform or may be expected to perform exposure prone procedures
- Diagnosis of another infection which shares a mode of acquisition with HBV
- A person who reports a positive result from an HBV test not licensed in Australia
- On the diagnosis of other conditions that may be caused by HBV infection e.g. glomerulonephritis, vasculitis
- Patients undergoing chemotherapy or immunosuppressive therapy or treatment for hepatitis C.

When a person requests an HBV test but does not disclose risk factors, their choice should be recognised and HBV testing provided.

Test interpretation

Two classes of assays are used in the diagnosis of HBV infection: serologic assays that detect specific HBV antigens and antibodies; and molecular assays that detect viral nucleic acid. For further details of testing contact the pathology provider or jurisdictional laboratory (refer to Appendix 4).

Hepatitis B surface antigen (HBsAg) can be detected in serum from several weeks before the onset of any illness. Other detectable markers of current (as opposed to resolved) HBV infection include HBV DNA and hepatitis B e antigen (HBeAg). Persistence of HBsAg denotes infectivity, which is generally greater if HBeAg is present and/or the HBV DNA viral load is high (34).

The presence of HBeAg and/or high hepatitis B DNA are markers of high infectivity. A falling concentration of HBeAg and rising anti-HBe correlates with reduced infectivity.

Anti-HBc IgM is present in high titre during acute infection and usually disappears within six months. However, anti-HBc IgM may also be detectable intermittently in those with chronic infection, such as during a hepatitis flare.

In the case of an acute infection that does not progress to chronic hepatitis B, seroconversion to anti-HBs may occur days, weeks or months after infection. Antibodies against HBsAg (anti-HBs) indicate immunity, which may result from either natural infection or immunisation. When immunity results from immunisation, there are no markers of current or past HBV infection such as anti-HBc.

People with chronic HBV infection are identified by the long-term presence (longer than six months) of HBsAg.

Table 1.Tests used for Hepatitis B infection

Marker	Abbreviations	Purpose or uses
Hepatitis B surface antigen (qualitative)	HBsAg	Donor testing – screening of blood and tissue donations
Hepatitis B surface antigen (qualitative)		Diagnostic testing - marker of current infection
Hepatitis B surface antigen neutralisation		Confirmation of the presence of HBsAg
Hepatitis B surface antigen (quantitative)	HBsAg	Monitoring of therapy, particularly with regard to interferon-based treatment – currently in a research context, not standard of care nationally
Hepatitis B surface antibody	anti-HBs or HBsAb	Usually indicates immunity, either from past infection or immunisation. Anti-HBs levels may decline to undetectable levels over years, especially if resulting from immunisation.
Hepatitis B core total antibody	anti-HBc or	Evidence of infection with HBV
	HBcAb	Marker of past or present infection. Generally remains detectable for life even if infection clears. Vaccination does not produce anti-HBc
IgM to hepatitis B antigen	IgM anti-HBc or HBcIgM	Suggestive of acute infection in the recent past (usually less than six months). Can also be detected during a flare of chronic hepatitis B.
Hepatitis B e antigen	HBeAg	Determining infectivity of a person with HBV infection and phase of the infection for clinical management Marker of enhanced infectivity. Seen transiently in most infections, and persists in some with chronic infection for many years. Absence of HBeAg does not exclude a high level of infectivity or disease activity, however (e.g. in the presence of pre-core mutants).
Hepatitis B e antibody	Anti-HBe or HBeAb	Marker of seroconversion from HBeAg, and stage of infection for clinical management
Hepatitis B DNA (qualitative)	HBV DNA	Donor testing – screening of blood and tissue donations Confirm the presence of circulating HBV
Hepatitis B DNA	HBV DNA VL	A quantitative measure of viral load and infectivity. An important investigation to establish phase of infection, monitor disease activity, and assess ongoing response to treatment and treatment adherence.
Hepatitis B sequencing – genotyping and resistance testing		Characterisation of virus for clinical management. Used to assess presence of mutations conferring antiviral resistance. Genotyping also occasionally used to determine likelihood of responding to interferon-based therapy but this is not standard of care nationally. Other public health uses e.g. transmission investigations.

Further information is available in the National Hepatitis B Testing Policy, refer to the Testing Portal, and also from the Australasian Society for HIV Medicine resource, *Interpreting hepatitis B serology: Recommended wording for national laboratories to report hepatitis B diagnostic test results, refer to the ASHM website.*

9. Case management

Response times

Public health action should commence within three working days of notification of a confirmed case of newly acquired HBV infection. The timing of the public health response to cases of unspecified HBV infection is at the discretion of the public health unit.

Response procedure

Determining the source of infection for newly acquired cases may permit identification of other cases and interrupt infection transmission.

Case investigation

The response to a notification will usually be carried out in collaboration with the case's clinical team. PHU staff should assist by investigating the likely source of infection, and determining whether the case is newly acquired or unspecified for surveillance purposes. This will require engagement with the clinical team and sometimes the case or caregiver.

Public health staff should confirm that action has been taken to:

- Confirm that the case meets the case definition. Confirm the onset date, symptoms and signs of illness, and assess whether the clinical evidence is consistent with a diagnosis of hepatitis B
- Discuss with the treating clinician the need to interview the case or the relevant care giver in order to provide information and to seek a contact history; and seek the clinician's permission to do so
- Establish what the case or the relevant care-giver has already been told about the diagnosis before beginning the interview
- Confirm results of existing relevant laboratory tests, or recommend that the tests be done
- Review case and contact management undertaken to date
- Seek complete core and enhanced data (where relevant) on the case.

Case classification: Among the many cases classified by the NNDSS case definitions as unspecified HBV infection there may be a small proportion which, with further information, may be properly classified as newly acquired HBV infection. Cases notified as HBsAg positive with no other results, and cases notified as HBsAg positive with both anti-HBc and HBcIgM negative may potentially be shown to be newly acquired HBV infection by further tests. Recommended follow-up actions are as follows.

If HBsAg positive and no other test results are available:

- Confirm that anti-HBc and anti-HBc IgM tests have *not* been done.
- Check for any previous HBsAg results
- If none, contact clinician recommending anti-HBc and anti-HBc IgM testing

If HBsAg positive and both anti-HBc and anti-HBc IgM are negative:

- Contact clinician recommending repeat testing.

Electronic laboratory reporting may already have prompted the recommended clarifying tests. If this process is known to be in place in the notifying laboratory, no further action is required.

The clinical and public health management of cases of acute or unspecified HBV infection may be facilitated by contact between clinical teams and the jurisdictional or regional PHU. This aims to assist clinicians with exposure investigation and contact tracing, improve testing and vaccination of household and sexual contacts when indicated, and improve completeness and quality of core epidemiological data. Further, in newly diagnosed chronic HBV infections, public health units can support non-specialist clinicians to access information sources on management and referral to improve long-term case outcomes.

In jurisdictions with large numbers of hepatitis B notifications, communication with the notifying clinician/s may be done with a standard letter (refer to Appendix 5), case report form, and other supporting information.

Exposure investigation

Newly acquired hepatitis B

Determining the source of infection of newly acquired cases may permit identification of other co-exposed cases and opportunities to interrupt further transmission.

Trace back by seeking information about exposures during the likely acquisition period from six weeks to six months before onset of the illness. A longer risk history may be needed for newly acquired cases identified through the detection of HBsAg within 24 months of a negative result. If the illness onset is unclear consider tracing back to six months before to the most recent negative result.

Unspecified hepatitis B infections

When chronic infection is diagnosed in a person who is likely to have been infected vertically, it is important that the mother and household contacts be tested. Other possible sources of cases of CHB infection are rarely useful to pursue.

An investigation checklist which includes a list of possible exposures is provided in Appendix 1.

Case treatment and monitoring

Discussing, offering and providing treatment for HBV are the responsibility of the case's clinician. Cases should be tested for other blood borne viruses (HCV, HDV and HIV).

Acute hepatitis B

For most patients, treatment for acute hepatitis B is mainly supportive. Patients with clinically severe illness, and those in at greater risk of worse outcomes (e.g. patients who are immunocompromised, also have hepatitis C virus infection, have pre-existing liver disease, or are older adults) should be referred for specialist care(35, 36). For the great majority of cases of acute hepatitis B, routine antiviral therapy is not supported by available evidence; however in some cases of fulminant acute hepatitis B, antiviral therapy may be administered. Rarely, individuals with fulminant acute hepatitis B require liver transplantation for liver failure.

Chronic hepatitis B

It is important to ensure that people with CHB establish a sustainable clinical relationship with a trusted primary healthcare provider, for chronic hepatitis monitoring and cancer screening, hepatitis treatment, and management of co-morbidities.

Treatment of CHB with pegylated interferon (PEG-IFN), or nucleoside/nucleotide analogues (eg. lamivudine, adefovir dipivoxil, telbivudine, entecavir, tenofovir) (37) has been shown to substantially reduce the risk of progressive liver disease, and antivirals can reduce the risk of liver cancer by over 50 per cent over 4-5 years (38). Over three quarters of Australians in 2014 were receiving treatment for CHB are receiving either entecavir or tenofovir (32). All people living with CHB should have regular monitoring of their disease activity so that specific treatment can be considered when indicated. Further information on the management of CHB is available from the HepBHelp website and from the ASHM B Positive resource. Surveillance for primary liver cancer is part of the management of CHB.

People with chronic HBV are at risk of serious and sometimes life-threatening disease flares during cancer chemotherapy, or other prolonged or significant immunosuppressive therapy. In addition, some profound immunosuppressive regimens (such as bone marrow or stem cell transplantation) can lead to reactivation of resolved (anti-HBc positive, HBsAg negative) HBV infection. The National Hepatitis B Testing Policy recommends all patients about to undergo significant immunosuppression should be tested for HBV and referred to a specialist for consideration of close monitoring or antiviral treatment as appropriate, refer to the ASHM B Positive website and the ASHM Testing Portal on National HBV testing policy.

Direct-acting antiviral (DAA) medicines used to treat chronic hepatitis C virus (HCV) infection have also been associated with reactivation of HBV in patients with current or past HBV infection. This risk can be mitigated by advising HCV patients of this issue, screening for current or past HBV infection (including HBsAg and anti-HBc), and carefully monitoring liver function during DAA treatment, refer to the TGA website.

Education

Inform the case or care-giver of measures to prevent HBV transmission, including:

- Cleaning and disinfection of surfaces contaminated with blood
- Not sharing objects potentially contaminated with blood (for example razors and toothbrushes, injecting equipment)
- Single use of disposable needles
- Storing contaminated sharps in an approved sharps container
- Covering any wound with an impermeable dressing
- Practising safe sex
- Not donating blood or body parts.
- Immunisation of contacts, including sexual partners, as indicated (refer below).

HBsAg-positive people who seek medical or dental care may be encouraged, but are not obliged, to inform involved personnel of their hepatitis B status.

Provide the case and (with their permission) their family and other potentially exposed individuals an information sheet on hepatitis B infection. Consider using an interpreter with cases or contacts from a non-English speaking background, or an Aboriginal Health Education Officer for Aboriginal people. The information sheet should provide information about the nature of the infection, the mode of transmission, and preventive measures (refer to Appendix 3 for an example information sheet) and be written in an appropriate language (information sheets in different languages are available at the ASHM hepatitis B resources page.

Isolation and restriction

Isolation of people living with CHB is not required. The infected person should be educated about transmission routes, safe injecting and sexual practices, blood and body fluid precautions, and not donating organs or blood.

Child care

There are no restrictions on a child living with hepatitis B from attending childcare. The risk of transmission of HBV in child care settings is very low, given universal vaccination of children in Australia. Sound infection control and environmental cleanliness and appropriate management of blood and body fluid spills, further reduces this risk. Further information is available in *Staying Healthy: Preventing infectious diseases in early childhood education and care services*, 5th Edition.

Healthcare settings

Hospitalised cases of acute or chronic HBV infections do not need to be isolated. The risk of secondary cases from hospitalised cases can be prevented by standard and transmission-based precautions, pre-exposure hepatitis B vaccination of staff, and post-exposure management of potentially exposed healthcare workers

For healthcare workers infected with HBV – refer to section 12, Special situations.

10. Environmental investigation

Despite the fact HBV is stable on surfaces and infective for at least seven days under experimental conditions (39), it is readily inactivated by most disinfectants. Environmental sources are rarely, if ever, the source of infection, and therefore environmental investigation is generally not indicated, except when a cluster of cases is reported that raise the possibility of an environmental source.

11. Contact management

Contacts may be the source of infection for the case, or may be at risk of infection from the case.

The aim of contact management is to prevent or minimise illness among contacts, and to prevent ongoing transmission from existing or potential new sources of infection.

The clinician managing the patient is usually responsible for initiating the tracing and management of contacts. PHU staff may contact the clinician directly or by letter to emphasise the need for testing and vaccination of household and sexual contacts, and advise on the availability of state-funded vaccine. The clinician may be assisted by PHU staff and others, such as sexual health service staff, in accordance with local processes. The *Australian Contact Tracing Manual* provides guidance , refer to the ASHM website and the Northern Territory hepatitis B vaccination and public health guidelines.

Contact tracing must be done with regard to legal, ethical and confidentiality considerations. This includes the requirement to seek permission from a case if it is deemed necessary to disclose their identity to manage the risk to contacts.

Management of contacts includes:

- Noting the requirement to obtain consent from the case to disclose their identity (as above), clarify the timing and nature of their contact with the case and their risk of infection
- Alert them to the possibility that they could already be, or may become, infected, and recommend testing
- Arrange tests including HBsAg, anti-HBs, anti-HBc (total) and, if suspecting acute infection, anti-HBc IgM. Refer to Table 1 (above)
- If no evidence of immunity from previous infection (positive anti-HBc) or vaccination (anti-HBs level ≥10 mIU/mL documented at any time after previous vaccination), and depending on circumstances and timing, recommend active immunisation with or without passive immunisation (refer to Table 2)
- Provide contacts with information about hepatitis B infection and their level of risk, aiming to allay unnecessary concern, ensure appropriate prophylaxis, and ensure appropriate action if they develop symptoms.

Contact definition

Contacts include:

- household members of a case
- sexual partners of a case
- newborn or infant of a HBsAg positive mother
- children of cases

- people who have shared injecting equipment with the case
- recipients of the blood or organs of the case which were collected while the case was potentially infectious
- people with exposure to blood or body fluids of the case (mucosal contact, sharps injury etc).

Prophylaxis

For immunisation details, refer to current *the Australian Immunisation Handbook .*

Passive immunisation

Passive immunisation with Hepatitis B Immune Globulin (HBIG) is used, along with active immunisation with hepatitis B vaccine, to provide post-exposure protection against HBV. HBIG should be given as soon as possible after exposure, and can be given up to 72 hours after the exposure. The exposed person's prior history of HBV infection, vaccination, and vaccine response status (if known) should always be considered, but treatment should not be unduly delayed whilst awaiting test results.

Post-exposure prophylaxis with HBIG is recommended for non-immune people in the following situations (refer to Table 2):

- Perinatal exposure to an HBsAg-positive mother
- Percutaneous, parenteral or permucosal exposure to infectious blood
- Sexual exposure to an HBsAg-positive individual.

Active immunisation

Active vaccination reduces the risk of perinatal HBV transmission (by 50 to 72%) if given very soon after birth (40-42). Active vaccination is also recommended for all non-immune people at risk who are identified in the course of a HBV case investigation. Post-vaccination serological testing 4-8 weeks after vaccination is recommended for sexual and household contacts and healthcare workers to assess their immunity. HIV-positive adults, and other immunocompromised adults including those with renal failure, may be at increased risk of acquiring HBV infection and also respond less well to vaccination. The Australian Immunisation Handbook outlines options to improve the serological response in immunocompromised adults and non-responders (26). For children born to mothers living with CHB, serological testing is recommended at least 3 months after the final dose of hepatitis B vaccine (refer to Table 2). Note that timelines in this table are considered ideal but if a longer period has elapsed, then vaccination is still protective for future contact.

Table 2: Public health management of contacts of hepatitis B cases (sourced from the Australian Immunisation Handbook 10th Edition)

Contact category	Hepatitis B immunoglobulin (HBIG)		Vaccine		Post-treatment testing
	Timing	Dose	Timing	Dose	
Perinatal (exposure of babies during and after birth)	Single dose immediately after birth (preferably within 12 hours of birth and certainly within 48 hours)	100 IU by IM injection	Immediately after birth (preferably within 24 hours, no later than 7 days), then at 2, 4 and 6 months of age[1]	0.5 mL, by IM injection	At least 3 months after final dose of vaccine
Household, mucosal or percutaneous (includes health care workers, after needle-stick injury, sharing injecting equipment, etc.)	Single dose within 72 hours of exposure	400 IU by IM injection; 100IU if Body Weight <30 kg	Within 7 days of exposure and at 1 and 6 months after 1st dose[1]	0.5 mL or 1 mL (depending on age), by IM injection	4-8 weeks after vaccination
Sexual	Single dose within 72 hours of last sexual contact (There is limited evidence for efficacy if given within 14 days of contact; however, administration as soon as possible after exposure is preferred. 100 IU if body weight <30 kg).	400 IU by IM injection;	Within 14 days and at 1 and 6 months after 1st dose[1]	0.5 mL or 1 mL (depending on age), by IM injection	4-8 weeks after vaccination

[1] The first dose can be given at the same time as HBIG, but should be administered at a separate site. Administration as soon as possible after exposure is preferred

Education

Advise susceptible contacts (or their parents/guardians) of the risk of infection, the need for immunisation; and to watch for symptoms of hepatitis occurring within six months of exposure.

Isolation and restriction

Remind contacts of the need to practise safe sex and/or safe injecting practices to minimise the risk of acquiring or transmitting infection, particularly until laboratory testing clarifies their immunity or infectious status. If they are found to be infected with HBV, refer to advice in Case management (Section 9).

12. Special situations

Pregnant women and their children

Advise women with CHB who are pregnant or of reproductive age about the risk of transmitting hepatitis B to a newborn child, and of the importance and effectiveness of immunisation to prevent transmission and infection.

Appropriate follow-up of a woman diagnosed antenatally is essential to ensure adequate clinical care of the mother, testing and vaccination of household contacts, and protection of the infant from vertical transmission. Women with a positive HBsAg test on antenatal screening should be referred to specialist services to assist in their management, including consideration of antiviral therapy to further reduce the risk of vertical transmission in the setting of a high HBV DNA viral load (e.g. over 1 million IU/mL).

Infants born to HBsAg-positive mothers should be given HBIG and a dose of monovalent hepatitis B vaccine as soon as possible on the day of birth, concurrently but in separate thighs. Mothers delivering outside of institutions (e.g. home delivery) must have arrangements made for this to be provided, such as through a general practitioner (GP). Three subsequent doses of a hepatitis B-containing vaccine should be given, at 2, 4 and 6 months of age. Anti-HBs antibody and HBsAg levels should be measured in infants born to mothers with CHB infection 3 to 12 months after completing the primary vaccine course. If anti-HBs antibody levels are adequate (≥10 mIU/mL) and HBsAg is negative, then the infant is protected. If the anti-HBs level is <10 mIU/mL, then the possibility of HBV infection should be investigated. Refer to section 4.5.7 of *The Australian Immunisation Handbook* 10th Edition for details.

Healthcare workers

Healthcare workers known to be infected with blood-borne viruses should be assessed and monitored in accordance with the *Australian National Guidelines for the Management of Health Care Workers known to be Infected with Blood-Borne Viruses.* Referral to a specialist is recommended for ongoing assessment and monitoring of healthcare workers with chronic HBV infection. Healthcare workers should be provided with a fact sheet on Hepatitis B and advised of their obligations with regard to exposure prone procedures (EPP) as detailed in the *Australian National Guidelines for the Management of Health Care Workers known to be Infected with Blood-Borne Viruses*.

If a person with newly diagnosed acute or chronic HBV infection is a healthcare worker who performs exposure-prone procedures, the need for a look-back investigation should be considered by the relevant jurisdictional agency with reference to the *Australian National Guidelines for the Management of Health Care Workers known to be Infected with Blood-Borne Viruses*.

Non-immune healthcare workers who perform exposure-prone procedures and who experience a percutaneous or mucosal exposure to an infectious source of HBV should have their exposure assessed and management initiated urgently by an expert clinician. The exposure may take place in or out of work setting. This may involve advice regarding the need to modify work practices involving exposure prone procedures, in accordance with national, jurisdictional and organisational guidelines, during the period of possible seroconversion and infection.

Non-immune healthcare workers who perform exposure prone procedures should be tested according to the *Australian National Guidelines for the Management of Health Care Workers known to be Infected with Blood-Borne Viruses.* (43).

Suspected healthcare acquired infection

If acute hepatitis B is diagnosed in a person, particularly with no identified risk factors for HBV infection, and the initial investigation suggests the possibility of healthcare acquired infection, initiate an investigation and notify the relevant jurisdictional agency. Keep in mind the possibility of other undisclosed sources of infection.

Blood transfusion and transplantation

The Australian Red Cross Blood Service (ARCBS) should be notified immediately if a case of acute of CHB has donated blood or plasma while possibly infectious, or if transfused blood or blood products are suspected as the possible source of infection. If a case occurs in a recipient of a tissue or organ transplant, the relevant transplant unit should be immediately informed.

Cluster of cases

If cases of acute HBV infection are found to be clustered in place or time, or have common exposures, an investigation should seek to identify the source of infection to inform preventive public health action. Early laboratory characterisation (including genotyping) may assist in assessing the relatedness of cases.

13. References and additional sources of information

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Further information

The Gastroenterological Society of Australia website
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The National Hepatitis B Testing Policy http://testingportal.ashm.org.au/hbv

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HIV, viral hepatitis and STIs: a guide for primary care (particularly Chapter 12)
http://www.ashm.org.au/resources/Pages/1976963411.aspx

National Health and Medical Research Council, Australian Guidelines for the Prevention and Control of Infection in Healthcare (2010)
https://www.nhmrc.gov.au/guidelines-publications/cd33

Staying Healthy: Preventing infectious diseases in early childhood education and care services, 5th Edition
http://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/ch55_staying_healthy_childcare_5th_edition_0.pdf

Hep B Help .org.au – Providing information and advice to GPs on the further investigation and management of patients with hepatitis B. http://www.hepbhelp.org.au/

ASHM hepatitis B resources page

http://www.ashm.org.au/HBV/prevention-testing-and-diagnosis-hepb/

WHO WPRO hepatitis data and Statistics
http://www.wpro.who.int/hepatitis/data/hepatitis_data_statistics/en/

National Centre for Immunisation Research & Surveillance (NCIRS)
http://www.ncirs.edu.au/provider-resources/vaccination-history/

The Australian Immunisation Handbook
http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10part4~handbook10-4-5

Department of Health PHLN web page
http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-phlncd-hepb.

Department of Health case definitions http://www.health.gov.au/casedefinitions

RANZCOG statement on the management of hepatitis B in pregnancy

https://www.ranzcog.edu.au/RANZCOG_SITE/media/RANZCOG-MEDIA/Women%27s%20Health/Statement%20and%20guidelines/Clinical-Obstetrics/Management-of-Hepatitis-B-in-Pregnancy-(C-Obs-50)-Review-July-2016.pdf?ext=.pdf

Interpreting hepatitis B serology: Recommended wording for national laboratories to report hepatitis B diagnostic test

results.http://www.ashm.org.au/Documents/Interpreting_HBV_Serology_FINAL.pdf

Therapeutic Goods Administration Safety advisory – risk of hepatitis B reactivation

https://www.tga.gov.au/alert/direct-acting-antiviral-medicines

Northern Territory hepatitis B vaccination and public health guidelines

http://digitallibrary.health.nt.gov.au/prodjspui/bitstream/10137/710/1/Northern%20Territory%20Hepatitis%20B%20Public%20Health%20Guidelines.pdf

Australian National Guidelines for the Management of Health Care Workers known to be Infected with Blood-Borne Viruses

http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-cdna-bloodborne.htm